REMARKS

Applicant respectfully requests that the foregoing amendments be made prior to examination of the present application.

As noted in the response filed November 25, 2002, the amended claims still obviate the rejections previously of record. In particular, all of the documents describe the use of bispecific antibodies and radiolabelled bivalent haptens, and none of them disclose or suggest administering a bi-specific antibody or antibody fragment having at least one arm that specifically binds a targeted tissue and at least one other arm that specifically binds a targetable conjugate and a first targetable conjugate which comprises a carrier portion and one or more conjugated enzymes, wherein said carrier portion comprises or bears at least one epitope recognizable by said at least one other arm of said bi-specific antibody or antibody fragment, and then administering either (1) a prodrug, when said enzyme is capable of converting said prodrug to a drug at the target site; or (2) a drug which is capable of being detoxified in said patient to form an intermediate of lower toxicity, when said enzyme is capable of reconverting said detoxified intermediate to a toxic form, and, therefore, of increasing the toxicity of said drug at the target site, or (3) a prodrug which is activated in said patient through natural processes and is subject to detoxification by conversion to an intermediate of lower toxicity, when said enzyme is capable of reconverting said detoxified intermediate to a toxic form, and, therefore, of increasing the toxicity of said drug at the target site, or (4) a second targetable conjugate which comprises a carrier portion which comprises or bears at least one epitope recognizable by said at least one other arm of said bi-specific antibody or antibody fragment, and a prodrug, when said enzyme is capable of converting said prodrug to a drug at the target site. Accordingly, Applicants respectfully submit that the present claims still are patentable over the previously cited documents.

In an Advisory Action dated January 2, 2003, the examiner indicated that claims 1, 30, 51 and 52 were allowable. All other claims depend from these claims, and therefore the application should be in condition for allowance. Favorable consideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date March 27, 2003

By Barbara G M. Dowell Reg. 43,640

for Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264

FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5143
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Twice Amended) A method of treating diseased tissues in a patient, comprising:

(A) administering to said patient a bi-specific antibody or antibody fragment having at least one arm that specifically binds a targeted tissue and at least one other arm that specifically binds a targetable conjugate;

(B) optionally, administering to said patient a clearing composition, and allowing said composition to clear non-localized antibodies or antibody fragments from circulation;

(C) administering to said patient a first targetable conjugate which comprises a carrier portion and one or more conjugated enzymes, wherein said carrier portion comprises or bears at least one epitope recognizable by said at least one other arm of said bi-specific antibody or antibody fragment; and

(D) administering to said patient [a second targetable conjugate which comprises a carrier portion and a prodrug, wherein said carrier portion comprises or bears at least one epitope recognizable by said at least one other arm of said bi-specific antibody or antibody fragment]

(1) a prodrug, when said enzyme is capable of converting said prodrug to a drug at the target site; or

(2) a drug which is capable of being detoxified in said patient to form an intermediate of lower toxicity, when said enzyme is capable of reconverting said detoxified intermediate to a toxic form, and, therefore, of increasing the toxicity of said drug at the target site, or

(3) a prodrug which is activated in said patient through natural processes and is subject to detoxification by conversion to an intermediate of lower toxicity, when said enzyme is capable of reconverting said detoxified intermediate to a toxic form, and, therefore, of increasing the toxicity of said drug at the target site, or

(4) a second targetable conjugate which comprises a carrier portion which comprises or bears at least one epitope recognizable by said at least one other arm of said bi-specific antibody or antibody fragment, and a prodrug, when said enzyme is capable of converting said prodrug to a drug at the target site.

30. (Twice Amended) A kit useful for treating diseased tissues in a patient comprising:

(A) a bi-specific antibody or antibody fragment having at least one arm that specifically binds a targeted tissue and at least one other arm that specifically binds a targetable conjugate;

(B) a first targetable conjugate which comprises a carrier portion and one or more conjugated enzymes, wherein said carrier portion comprises or bears at least one epitope recognizable by said at least one other arm of said bi-specific antibody or antibody fragment; [and]

(C) optionally, a clearing composition useful for clearing non-localized antibodies and antibody fragments; and

(D) [a second targetable conjugate which comprises a carrier portion and a prodrug, wherein said carrier portion comprises or bears at least one epitope recognizable by said at least one other arm of said bi-specific antibody or antibody fragment]

(1) a prodrug, when said enzyme is capable of converting said prodrug to a drug at the target site; or

(2) a drug which is capable of being detoxified in said patient to form an intermediate of lower toxicity, when said enzyme is capable of reconverting said detoxified intermediate to a toxic form, and, therefore, of increasing the toxicity of said drug at the target site, or

(3) a prodrug which is activated in said patient through natural processes and is subject to detoxification by conversion to an intermediate of lower toxicity, when said

enzyme is capable of reconverting said detoxified intermediate to a toxic form, and, therefore, of increasing the toxicity of said drug at the target site, or

(4) a second targetable conjugate which comprises a carrier portion which comprises or bears at least one epitope recognizable by said at least one other arm of said bi-specific antibody or antibody fragment, and a prodrug, when said enzyme is capable of converting said prodrug to a drug at the target site.

51. (Amended) The method of claim 1, wherein (D) comprises administering a prodrug and said enzyme is capable of converting said prodrug to a drug at the target site.

52. (Amended) The method of claim 1, wherein (D) comprises administering [said] a prodrug that is activated in said patient through natural processes and is subject to detoxification by conversion to an intermediate of lower toxicity, and said enzyme is capable of reconverting the detoxified intermediate to a toxic form, and, therefore, of increasing the toxicity of said drug at the target site.